Nkx2.5+ Cardiomyoblasts Contribute to Cardiomyogenesis in the Neonatal Heart.

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Public Summary:
During normal lifespan, the mammalian heart undergoes limited renewal of cardiomyocytes. While the exact mechanism for this renewal remains unclear, two possibilities have been proposed: differentiated myocyte replication and progenitor/immature cell differentiation. This study aimed to characterize a population of cardiomyocyte precursors in the neonatal heart and to determine their requirement for cardiac development. By tracking the expression of an embryonic Nkx2.5 cardiac enhancer, we identified cardiomyoblasts capable of differentiation into striated cardiomyocytes in vitro. Genome-wide expression profile of neonatal Nkx2.5+ cardiomyoblasts showed the absence of sarcomeric gene and the presence of cardiac transcription factors. To determine the lineage contribution of the Nkx2.5+ cardiomyoblasts, we generated a doxycycline suppressible Cre transgenic mouse under the regulation of the Nkx2.5 enhancer and showed that neonatal Nkx2.5+ cardiomyoblasts mature into cardiomyocytes in vivo. Ablation of neonatal cardiomyoblasts resulted in ventricular hypertrophy and dilation, supporting a functional requirement of the Nkx2.5+ cardiomyoblasts. This study provides direct lineage tracing evidence that a cardiomyoblast population contributes to cardiogenesis in the neonatal heart. The cell population identified here may serve as a promising therapeutic for pediatric cardiac regeneration.

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